REMARKS

The present application is directed to attenuation of pathangiogenic conditions by administering Group B β-hemolytic *Streptococci* (GBS) toxin receptors, or immunogenic fragments thereof, and is directed to related compositions and methods of producing the compositions. Applicant requests entry of amendments to Claims 1, 29-30, 32, 35, 40-42, 44-48 and 55 to overcome claim rejections or correct informalities and unintentional typographical errors. The amendments do not introduce any new matter. Claims 1, 4-16, 29-38, 40-48 and 55-56 will be pending upon entry of the amendments. Based on the amendments and the following remarks, applicant respectfully requests reconsideration and allowance of the claims.

Election/Restriction

Applicant wishes to thank the Examiner for rejoining Groups 1 and 11 from the Restriction Requirement of May 21, 2002, and withdrawing the requirement to elect a species.

Claim Rejections under 35 U.S.C. § 112, First Paragraph (Enablement)

In the Office Action mailed September 6, 2005, the Examiner maintained the rejection of Claims 1, 4-16, 30-38, 40-48, and 55-56 under 35 U.S.C. §112, first paragraph, for lack of enablement. Applicant respectfully submits that the amendments to the claims overcome the rejection.

Independent Claims 1, 29 and 55 have been amended to specify that the one or more GBS toxin receptors have an amino acid sequence substantially identical to HP59 or SP55. Support for this amendment can be found, for example, on page 7, lines 8-11.

The Examiner cites several publications for the proposition that rodent models may not represent clinical efficacy in humans. Applicant agrees that, although many of the newly cited publications recognize the value of mouse models, some call for the careful selection of

such models and require that certain limitations be taken into account when predicting the efficacy of preclinical animal-tested cancer therapies in humans. However, applicant respectfully submits that U.S. Patent laws fail to require a rigorous correlation between animal models and the success of the claimed method in humans. See *Cross v. Iizuka*, 753 F.2d 1040, 1050 (Fed. Cir. 1985). A demonstration of the effectiveness of a drug is not required for obtaining a patent. See *In re Brana*, 51 F.3d 1560, 1567 (Fed. Cir. 1995). Applicant respectfully asserts that the disclosure provided in the specification of the present application enables one skilled in the art to make and use the GBS toxin receptor compositions and methods having an amino acid sequence substantially identical to HP59 or SP55 as claimed.

In addition to the amendments to the claims, applicant submits the enclosed Second Declaration of Carl Hellerqvist under 37 C.F.R. §1.132. This Declaration concludes that observations in appropriately selected mouse models reasonably correlate with observations in other mammals, such as humans. Applicant respectfully asserts that the mouse models used in the Examples of the present application were selected so they reasonably correlate with human pathological angiogenesis to demonstrate the ability of GBS toxin receptors having an amino acid sequence substantially identical to HP59 or SP55 to attenuate pathological angiogenesis associated with cancer in a mammal as now claimed. As explained in the enclosed Declaration, mouse models correlate with results in other mammals in the claimed methods because "pathological angiogenesis associated with cancer" targets pathological vasculature that is common between mice and humans.

The enclosed Declaration describes multiple studies in which applicant demonstrated the correlation of the effects of GBS toxin administration in both mouse cancer models and human patients. By cloning and identifying HP59, the target protein for GBS toxin/CM101 in humans and sheep, and by immunohistochemical studies in mice, applicant showed the existence of a conserved molecular marker for neonatal and pathologic vasculature in mammals. See Fu *et al.* (2001). Applicant also showed that HP59 is present in the tumor vasculature independently of site and type. See Table 1 in Fu *et al.* All antibodies generated

to the human and sheep HP59 analogue cross-reacted with pathologic vasculature in mice. Thus, the HP59 protein is a pathologic vasculature target common between humans, sheep and mice.

As further discussed in the enclosed Declaration, applicant showed that administration of HP59 protein generates a cellular immune response that inhibits pathologic angiogenesis. Thus, applicant identified HP59 as a target for attenuating cancer-associated pathologic angiogenesis in various mammalian tissues.

It is applicant's position that, in the field of cancer vaccines, mouse models are considered to correlate reasonably well with human pathological angiogenesis conditions, such as those associated with cancer. Although the Examiner cited several publications in the present Office Action as evidence against applicant's position, the cited publications predominantly focus on the limitations of mouse models for predicting clinical outcomes during development of drugs targeting various tumor-specific targets, not treatments directed at pathological vasculature-specific targets. For example, Wang *et al.* (2001), cited by the Examiner, describes the use of anti-cancer vaccines against tumor-specific antigens. Accordingly, the cited publications are not relevant to applicant's claimed method.

Genetic and phenotypical diversity of tumor tissues makes tumor-specific targeting difficult. This diversity negatively influences the correlation between mouse models and humans when tumor targets are affected. In contrast, one of ordinary skill in the art expects reasonable correlation between animal models and humans when targeting cancer-associated pathologic vasculature, provided that the vascular target is common in the model animal and humans. At least one reason for the expected reasonable correlation between animal models and humans when testing therapies that target pathologic vasculature is that such vasculature is relatively genetically and phenotypically homogenous. Applicant selected a mouse model to demonstrate the claimed methods because mouse vasculature possesses the same target as human and sheep vasculature. Therefore, one of ordinary skill in the art would expect that the mouse models utilized in the present application would reasonably correlate with human

results for the purpose of observing angiogenesis inhibition in accordance with applicant's method.

In the present application, applicant's method and compositions target a protein common to the pathologic vasculature of various types of tumors and shared by at least humans, mice, and sheep. Applicant also elucidated the common mechanism of action of GBS toxin during angiogenesis. Based on the foregoing and on the previously submitted arguments, applicant maintains that the attenuation of cancer-associated angiogenesis in the mouse models used in the working examples of the present application correlates with human pathologic angiogenesis associated with conditions such as cancer due to the presence of common CM101 target proteins in mice and humans and common mechanism of action. For at least the foregoing reasons, applicant respectfully requests withdrawal the rejection under 35 U.S.C. § 112, first paragraph.

Claim Rejections under 35 USC §112, Second Paragraph

The Examiner rejected Claims 1, 4-16, 29-38, 40-48, 55 and 56 under 35 USC §112, second paragraph, as indefinite. Applicant respectfully submits that the amendments to the claims overcome the rejection.

In particular, the Examiner rejected the claims on the basis that the language "wherein the pathoangiogenic condition comprises cancer" was indefinite. The claims have been amended to replace the language "wherein the pathoangiogenic condition comprises cancer" with the phrase "pathological angiogenesis associated with cancer."

In addition, the Examiner rejected the claims on the basis that the language "comprises HP59 or SP55" was indefinite. Claims 1, 29, 30 and 55 have been amended to clarify that the Group B β-hemolytic *Streptococci* toxin receptor has an amino acid sequence substantially identical to HP59 or SP55, or immunogenic fragment thereof. Support for this amendment is found at least on p. 8, line 28, through p. 9, line 25.

For at least the foregoing reasons, applicant asserts that claim amendments overcome the rejection under 35 U.S.C. §112, second paragraph, as indefinite and requests withdrawal thereof.

Rejections under 35 USC §112, First Paragraph (Written Description)

The Examiner rejected Claims 1, 4-16, 29-38, 40-48, 55 and 56 under 35 USC §112, first paragraph, as failing to comply with a written description requirement on the basis that the specification does not support the genus of polypeptides of GBS toxin receptors or immunogenic fragments thereof as recited in the rejected claims.

As discussed above, applicant has amended the claims to clarify that the GBS toxin receptor has an amino acid sequence substantially identical to HP59 or SP55. Applicant asserts that the specification provides sufficient written description for the genus recited in the claims by providing a description of a representative number of species, by actual reduction to practice, and by disclosure of relevant, identifying characteristics sufficient to show that applicant was in possession of the claimed genus. Applicant disclosed the amino acid and nucleic acid sequences for HP59 and SP55 (see Table 1 in the specification), two Group B β-hemolytic *Streptococci* toxin receptors whose features are defined, for example, on page 6, lines 26-30 of the specification. Applicant described how to identify other GBS toxin receptors using the HP59 and SP55 nucleic acid sequences on page 19, line 14, through page 22 of the specification.

The HP59 and SP55 nucleic acid sequences provided in the present application are relevant characteristics that allow one of ordinary skill in the art to readily identify other members of the genus of Group B β-hemolytic *Streptococci* toxin receptor substantially identical to HP59 or SP55. Accordingly, the specification provides sufficient written description for the genus of Group B β-hemolytic *Streptococci* toxin receptors substantially identical to HP59 or SP55. The specification also provides sufficient written description for the genus of the immunogenic GBS toxin receptor fragments. Specifically, in Tables 3 and

4, a number of immunogenic peptides (Hab 1, Hab2, Hab 3, Hab 4, p55a, p56a and p57) are provided. Table 2 provides three more regions of SP55 that are likely to be immunogenic.

Accordingly, applicant respectfully assert that the specification of the present application in combination with knowledge available to one of ordinary skill in the art at the time of filing of the present application would reasonably convey to the skilled artisan that applicant had possession of the claimed invention at the time the application was filed. For at least the foregoing reasons, applicant respectfully requests withdrawal of the rejection under 35 U.S.C. §112, first paragraph, as failing to comply with a written description requirement.

Rejection of Claims under 35 USC §102(e)

Claims 29-34, 37, 38, 40-43, 45-48, 55, and 56 were rejected by the Examiner under 35 U.S.C. §102(e) as anticipated by U.S. Patent No. 6,803,448 ("the '448 patent") to Carl G. Hellerqvist and Changlin Fu. Applicant respectfully submits that the '448 patent is not a valid prior art reference.

Applicant submits herewith a "*Petition for Unintentionally Delayed Claim of Benefit of Earlier Filing Date*" to claim the benefit of currently pending U.S. Patent Application Serial No. 10/823,506, which is a divisional application of U.S. Patent Application Serial No. 09/359,167, now issued as U.S. Patent No. 6,803,448. Accordingly, upon granting of the Petition, U.S. Patent No. 6,803,448 is not prior art within the meaning of 35 USC §102(e) and applicant requests withdrawal of the rejection.

Obviousness-type Double Patenting Rejection

The Examiner rejected Claims 29-32, 38, 40-43, 45-47 and 55 over U.S. Patent No. 6,803,448 to Hellerqvist under the doctrine of obviousness-type double patenting. Applicant submits that, when allowable subject matter is found in the present application, applicant will file, if appropriate, a terminal disclaimer disclaiming the part of the term of a patent to issue from the present application extending beyond the term of U.S. Patent No. 6,803,448.

Other Issues

The Examiner appeared to require, on page 19 of the Office Action, a showing that the inventions claimed in the present application and in U.S. Patent No. 6,803,448 were commonly owned at the time of the invention in order to fulfill the provisions of 35 U.S.C. § 103(c) and 37 C.F.R. 1.78(c). Applicant submits that, upon granting of *A Petition for an Unintentionally Delayed Claim of Benefit of Earlier Filing Date*, this requirement will be moot. If applicant misunderstood the relevant section of the Office Action, clarification is respectfully requested.

CONCLUSION

Applicant is of the opinion that the Office Action has been completely responded to and that the application is now in condition for allowance. Such action is respectfully requested. No additional fees are believed due, however, the Commissioner is hereby authorized to charge any deficiencies that may be required or credit any overpayment to Deposit Account Number 11-0855.

If the Examiner believes any informalities remain in the application that may be corrected by Examiner's Amendment, or there are any other issues that can be resolved by telephone interview, a telephone call to the undersigned at (404) 815-6102 is respectfully solicited.

Respectfully submitted,

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